

Appl. No. : **09/076,404**
Filed : **May 12, 1998**

REMARKS

Claim Status and Amendments

The Advisory Action mailed June 25, 2007 notes that the amendments filed June 11, 2006 were not entered. Accordingly, the claims amendments provided herein are with respect to the most recently entered amendments, which were filed on October 17, 2006.

Following entry of the amendments submitted herewith, claims 19, 20, 26, 30, 32, 33, 34, 35, 37, 38, 40, 41, 43, 44, 46, and 47 will be pending. Claims 21-25, 27-29, 31, 36, 39, 42, and 45 are canceled. Claims 19, 26, 30, 32, 34, and 40 are currently amended.

As support for the claim amendments and additions is found throughout the specification as filed, no new matter is added by way of these amendments and additions. As described in detail below, the specification as filed provides adequate support for human target RNAs having molecular interaction sites that are less than 30 nucleotides. Claims 19, 26, 32, and 34 are amended to incorporate the limitations of dependent claims 36, 39, 42, and 45, respectively. Claims 19, 26, 32, and 34 are further amended for clarity by the insertion of “thereby identifying said compound that binds to a human RNA target” at the end of each independent claim. Claims 19, 26, 32, and 34 are additionally amended for clarity to replace “generating *in silico* a virtual library of compounds predicted or calculated to interact with a molecular interaction site” with “generating *in silico* a virtual library of compounds and an *in silico* three dimensional representation of a molecular interaction site,” support for which can be found throughout the specification and claims originally filed; see for example pages 94-95 of the specification. Amendments to correct typographical errors are made to claims 26 and 40. Claim 30 is amended to correct a claim dependency error.

Specification

Applicants submit herewith an amendment to the specification to identify the nucleotide sequences at page 63 with sequence identification numbers. Applicants also provide herewith a corrected CRF copy of the Sequence Listing. Applicants respectfully submit that the nucleotide sequence disclosures of the instant specification are now in compliance with the requirements of 37 C.F.R. §§ 1.821-1.825.

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Discussion of Rejection Under 35 U.S.C. § 112

In the Office Action mailed December 11, 2006, claims 36-47 were rejected under 35 U.S.C. § 112 as allegedly failing to comply with the written description requirement. The Examiner rejected claims 36-47 asserting that the “claim(s) contain subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.” Specifically, the examiner asserted that those claims fail to satisfy 35 U.S.C. § 112, written description because they are allegedly “drawn to a method comprising in silico virtual library analysis of compounds that bind a human target RNA with an interaction site that is either less than 30 nucleotides in length or comprising a secondary structure that is a bulge, a loop, a stem, a hairpin, or a mismatch basepair.” The Examiner asserted that the specification does not describe human target RNA sequences with an interaction site that is either less than 30 nucleotides in length or comprising a secondary structure that is a bulge, a loop, a stem, a hairpin, or a mismatch basepair.

In the Advisory Action mailed June 25, 2007, the Examiner maintained the written description rejection, asserting that the IRE element of approximately 30 nucleotides does not provide support for a molecular interaction site that is less than 30 nucleotides, as recited in the instant claims. The Examiner acknowledged that “the IRE element is shown to comprise an interaction site in an untranslated region, as claimed in claims 38, 41, 44, and 47, but those claims require the full scope of claims 37, 40, 43, and 46, which require an interaction site that is a bulge, a loop, a stem, or a mismatch repair which is not described in the context of the claims as a whole.” See Advisory Action at page 2.

Applicants respectfully disagree with the Examiner’s assertion that claims 36-47 fail to comply with the written description requirement. The limitations of claims 36, 39, 42, and 45 have been incorporated into claims 19, 26, 32, and 34, respectively. Accordingly, Applicants will address the rejection as it applied to the claims as amended. As discussed below, the Examiner has not shown by the requisite preponderance of the evidence that one of ordinary skill in the art would not reasonably conclude that Applicants were in possession of the invention as recited in any of the rejected claims.

To satisfy the written description requirement, a patent specification must describe the claimed invention in sufficient detail that one skilled in the art can *reasonably* conclude that the

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inventor had possession of the claimed invention (*Vas-Cath, Inc. v. Mahurkar*, 935 F.2d 1555, 1563, 19 USPQ2d 1111, 1116 (Fed. Cir. 1991), emphasis added). The initial burden of proof in establishing whether claims are supported by an adequate written description falls upon the Examiner, “The description as filed is presumed to be adequate, unless or until sufficient evidence or reasoning to the contrary has been presented by the examiner to rebut the presumption” (MPEP 2163.04 and *In re Marzocchi*, 439 F.2d 220, 224, 169 USPQ 367, 370 (CCPA 1971)). Furthermore, the Examiner “must have a reasonable basis to challenge the adequacy of the written description. The Examiner has the initial burden of presenting by a preponderance of the evidence why a person skilled in the art would not recognize in an applicant’s disclosure a description of the invention defined by the claims” (*In re Wertheim*, 541 F.2d at 263, 191 USPQ at 97 (CCPA 1976)).

The Examiner asserted that the “specification does not describe **human** target RNA sequences with an interaction site that is either less than 30 nucleotides in length or comprising a secondary structure that is a bulge, loop, a stem, a hairpin, or a mismatch basepair.” (emphasis in original) See Office Action at page 3. Claim 19 as amended recites a method of identifying a compound that binds to a human target RNA, comprising a step of generating an in silico three dimensional representation of a molecular interaction site within the human target RNA, wherein the molecular interaction site is less than 30 nucleotides. Claims 26, 30, and 32 recite a method of identifying a compound that binds to a human target RNA, comprising a step of identifying in silico at least one molecular interaction site less than 30 nucleotides in length on said human target RNA. Accordingly, the instant claims recite methods comprising a step of identifying a molecular interaction site, or alternatively a step of generating a three dimensional representation of a molecular interaction site.

The specification as filed provides several means for the identification of molecular interaction sites in target nucleic acids, including human target RNAs. For example, beginning at page 39, the specification describes numerous methods for the determination of secondary structure, including “self complementarity comparison, alignment and covariance analysis, secondary structure prediction, or a combination thereof.” The following paragraphs describe each of these methods in detail. At page 41, lines 8-15, the specification describes that the result of the secondary structure analysis is the identification of secondary structures, including bulges, loops, stems, hairpins, knots, triple interacts, cloverleafs, helices, or a combination thereof. The specification further describes the

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generation of a three dimensional structure of a molecular interaction site. For example, at pages 94-97, the instant specification discloses several means for the computational generation of molecular interaction site structures, including software programs.

As set forth in the instant specification, a molecular interaction site is “a region of a nucleic acid having a secondary structure” (see page 94) that is usually “less than 30 nucleotides.” (see page 16). The Examiner’s attention is drawn to Example 1, beginning at page 131, which describes the iron response element (IRE) that is a human RNA element of approximately 30 nucleotides that folds into a hairpin. As evidenced by Figure 13, the human IRE is 23 nucleotides in length, thus falling within the scope of the instant claims. Furthermore, as stated at page 133 of the specification, the IRE is located in an untranslated region (as recited in rejected claims 38, 41, and 47). Certain additional examples of human target RNAs are provided in Table 1 (pages 27-31). Accordingly, the specification, in addition to describing several means for identifying molecular interactions sites and generating three dimensional representations of molecular interaction sites, provides a specific example of a molecular interaction site suitable for use in the instantly claimed methods. The instant claims are not drawn to compositions comprising molecular interactions sites, but rather, methods comprising a step of identifying a molecular interaction site. Accordingly, one skilled in the art, armed with the disclosure of the instant specification, will be readily able to identify which of these molecular interaction sites are less than 30 nucleotides and further comprise a secondary structure or are present in an untranslated region of an RNA.

Applicants respectfully submit that in view of the various methods set forth in the specification for the identification and characterization of molecular interaction sites, the Examiner has no reasonable basis to challenge the adequacy of the written description.

Further, Applicants need not provide the sequence of each and every possible human target RNA to reasonably demonstrate that they were in possession methods for identifying a compound that binds to a human target RNA. In fact, it is well settled that working examples are not required to satisfy the written description requirement. For example, in *Falkner v. Inglis*, No. 05-1324 (US Court of Appeals for the Federal Circuit, May 26, 2006) the Federal Circuit concluded that:

- (1) examples are not necessary to support the adequacy of a written description
- (2) the written description standard may be met (as it is here) even where actual reduction to practice of an invention is absent; and
- (3) there is no per se rule that an

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adequate written description of an invention that involves a biological macromolecule must contain a recitation of the known structure.

The decision by the Federal Circuit in *Falkner* is in accordance with prior case law, including *Lizard Tech, Inc. v. Earth Resource Mapping, PTY, Inc.* 424 F.3d 1336, 1345 (Fed. Cir. 2005) and *Union Oil Co. v. Atlantic Richfield Co.* 208 F.3d 989, 997 (Fed. Cir. 2000), which concluded, “A claim will not be invalidated on section 112 grounds simply because the embodiments of the specification do not contain examples explicitly covering the full scope of the claim language.”

The well-established test for sufficiency of support under the written description requirement of 35 U.S.C. §112, first paragraph is stated by the Court in *Vas-Cath, Inc. v. Mahurkar*, 935 F.2d 1555, 19 U.S.P.Q.2d 1111 (Fed. Cir. 1991) “Although [the applicant] does not have to describe exactly the subject matter claimed . . . the description must clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed” (citations omitted). Upon reviewing the disclosure, which includes methods for identifying a molecular interaction site, methods for generating a three dimensional structure of a molecular interaction site, and at least one example of a human interaction site that is less than 30 nucleotides in length, and further comprising a secondary structure that is a bulge, a loop, a stem, a hairpin, or a mismatch basepair, one of skill in the art would recognize that Applicants were in possession of methods comprising in silico virtual analysis of compounds that bind to such human target RNAs. One of skill in the art would additionally recognize that Applicants were in possession of methods comprising in silico virtual analysis of compounds that bind a human target RNA with a secondary structure located in an untranslated region of a human target RNA.

For at least these reasons, the Examiner has failed to meet the initial burden of establishing by a preponderance of the evidence that one of ordinary skill in the art would not reasonably believe that Applicants were in possession of the claimed invention. Applicants respectfully submit that the subject matter of the instantly claimed methods was adequately described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventors were in possession of the claimed invention at the time the application was filed. Accordingly, Applicants respectfully request withdrawal of the rejection under 35 U.S.C. § 112, first paragraph.

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In the Office Action mailed **December 11, 2006**, **claim 30** was rejected under 35 U.S.C. § 112 as being incomplete because it depends from cancelled claim 29. Claim 30 is herein amended to depend from claim 26 herein.

In the Advisory Action mailed June 25, 2007, the Examiner noted that the amendment to claim 30 would overcome this rejection if the amendment was entered. Applicants respectfully request that the Examiner enter the amendment and withdraw the rejection.

Discussion of Rejection Under 35 U.S.C. § 103(a)

In the Office Action mailed December 11, 2006, **claims 19, 20, 26, 32-35, 37, 38, 40, 41, 43, 44, 46, and 47** are rejected under 35 U.S.C. § 103(a) as allegedly being unpatentable over Murray et al. in view of Arenas et al. in view of Sezerman et al. in view of Greig et al in view of Scherly et al. in view of Petterson et al. in view of Lamond. Applicants respectfully disagree that the combination of these seven references teaches or suggests the claimed methods. However, in an effort to advance prosecution, claims 19, 26, 32 and 34 are herein amended to incorporate the limitations of dependent claims 36, 39, 42, and 45, respectively. The Examiner excluded claims 36, 39, 42, and 45 from the instant rejection, thereby indicating that these four claims are free of the prior art. Accordingly, Applicants submit that the claims as amended herein are not obvious in view of the cited references.

In the Advisory Action mailed June 25, 2007, the Examiner noted that the arguments concerning the rejection under 35 U.S.C. § 103(a) are based upon entry of the amendments and are therefore not persuasive in view of the non-entry of the amendment. Applicants respectfully request that the Examiner enter the amendments submitted herewith, and withdraw the rejection.

Double Patenting

Applicants note that claims 19-23 and 26-35 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 21-30 of copending application No. 10/104,949. Applicants would like to bring to the Examiner's attention that U.S. Application Serial No. 10/104,949 is abandoned. Accordingly, Applicants respectfully request withdrawal of this rejection.

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In the Advisory Action mailed June 25, 2007, the Examiner noted that the rejection on the grounds of nonstatutory obviousness-type double patenting was overcome, in view of the abandonment of U.S. Application Serial No. 10/104,949.

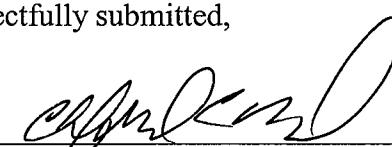
Conclusion

Applicants believe that all outstanding issues in this case have been resolved and that the present claims are in condition for allowance. Nevertheless, if any undeveloped issues remain or if any issues require clarification, the Examiner is invited to contact the undersigned at the telephone number provided below in order to expedite the resolution of such issues.

Please charge any additional fees, including any fees for additional extension of time, or credit overpayment to Deposit Account No. 50-0252.

Respectfully submitted,

Dated: 10/31/07

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